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PATENT APPLICATION
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HEPARAN SULFATE D-GLUCOSAMINYL 3-*O*-SULFOTRANSFERASES, AND USES THEREFOR

Cross-Reference to Related Application

~~This application claims benefit of priority of International Patent Application Serial No. PCT/US98/22597, with an international filing date of October 23, 1998, which claims priority to U.S. Provisional Patent Application Serial No. 60/062,762, filed on October 24, 1997, and U.S. Provisional Patent Application Serial No. 60/065,437, filed on October 31, 1997.~~

This application claims benefit of U.S. provisional application 60/062762 filed 10/24/1997 which is a continuation of PCT/US98/22597 filed 10/23/1998 which claims benefit of 60/062762 filed 10/24/1997 and claims benefit to US provisional application 60/065-437 filed 10/31/1997.

Field of the Invention

The present invention is related to the field of biochemistry and molecular biology, and in particular to the field of enzymology and heparan sulfate biosynthesis.

Background of the Invention

The serine proteases of the intrinsic blood coagulation cascade are slowly neutralized by antithrombin (AT) (reviewed in (1)). This inhibition is secondary to the generation of 1:1 enzyme-AT complexes whose formation is dramatically enhanced by the mast cell product, heparin (2). Damus *et al.* (3) hypothesized that endothelial cell surface heparan sulfate proteoglycans (HSPGs) function in a similar fashion to accelerate coagulation enzyme inactivation by AT, and therefore are responsible for the non-thrombogenic properties of blood vessels. It was initially demonstrated that perfusion of the hindlimbs of normal rodents and rodents deficient in mast cells with purified thrombin (T) and AT leads to a greatly elevated rate of T-AT complex formation and that the enzyme heparitinase as well as the natural heparin antagonist platelet factor 4 suppress the above acceleration (4, 5). It was subsequently showed that cultured cloned bovine macrovascular and rodent microvascular endothelial cells synthesize both anticoagulant HSPG ($HSPG^{act}$) as well as nonanticoagulant HSPG ($HSPG^{inact}$) (6-8). $HSPG^{act}$ bear glycosaminoglycan (GAG) chains that bind tightly to AT and accelerate T-AT complex generation (6-8).